II

110TH CONGRESS
1ST SESSION

S. 1505

To amend the Public Health Service Act to provide for the approval of biosimilars, and for other purposes.

IN THE SENATE OF THE UNITED STATES

MAY 24, 2007

Mr. GREGG (for himself, Mr. BURR, and Mr. COBURN) introduced the following bill; which was read twice and referred to the Committee on Health, Education, Labor, and Pensions

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A BILL

To amend the Public Health Service Act to provide for the approval of biosimilars, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE.

This Act may be cited as the ''Affordable Biologics for Consumers Act''.

SEC. 2. APPROVAL OF BIOSIMILARS.

(a) IN GENERAL.—Section 351 of the Public Health Service Act (42 U.S.C. 262) is amended—

(1) in subsection (j), by striking ''under subsection (a)'' and inserting ''under subsection (a) or (k)''; and

(2) by adding at the end the following:

''(k) BIOSIMILARS.—

''(1) APPLICATION.—

''(A) SUBMISSION.—Any person may submit an application under this subsection for approval of a biologics license for a biosimilar.

''(B) DEFINITIONS.—In this subsection:

''(i) BIOSIMILAR.—The term 'biosimilar' means a biological product that, in an application submitted under this subsection, is claimed to be similar to a qualified biological product (in this subsection referred to as the 'reference product').

''(ii) QUALIFIED BIOLOGICAL PRODUCT.—The term 'qualified biological product' means a biological product that is a biotechnology-derived therapeutic biological product licensed under subsection (a) or a biotechnology-derived therapeutic protein product subject to an approved application that was submitted under section

505(b)(1) of the Federal Food, Drug, and Cosmetic Act.

''(2) REVIEW AND APPROVAL OF BIOSIMILAR APPLICATIONS.—

''(A) REVIEW.—An application submitted under this subsection for a biosimilar shall be reviewed—

''(i) by the division that was responsible for review and approval of the reference product; and

''(ii) in accordance with the procedures for review of biologics license applications established by the Secretary pursuant to subsection (a)(2)(A).

''(B) APPROVAL.—The Secretary shall approve the application submitted under paragraph (1) only if—

''(i) the applicant demonstrates that the biosimilar conforms to the applicable final product class-specific rule and, on the basis of the data submitted in conformance with such rule, the Secretary concludes the product is safe, pure, and potent;

''(ii) the applicant demonstrates that the biosimilar is as similar to the reference

product as may be achieved given the state of scientific knowledge and technology capabilities at the time of submission of the application;

''(iii) the applicant demonstrates that the biosimilar has the same route of administration, dosage form, mechanism of action, and strength as the reference product;

''(iv) the facility in which the biosimilar is manufactured, processed, packed, or held meets standards designed to assure that the biological product continues to be safe, pure, and potent; and

''(v) the applicant (or other appropriate person) consents to the inspection of the facility that is the subject of the application, in accordance with subsection (c).

''(C) CONDITIONS OF APPROVAL.—The Secretary may approve an application submitted under paragraph (1) for a biosimilar—

''(i) only for indications for which the reference product is approved;

''(ii) only if, with respect to each such indication, the application conforms to the

applicable final product class-specific rule, and on the basis of non-clinical and clinical data submitted regarding such indication, the Secretary concludes the product is safe, pure, and potent; and

"(iii) only if the applicant agrees to provide to the Secretary, on an ongoing basis, all written documents it prepares for any purpose (including any patent litigation) that characterizes the difference between the biosimilar and the reference product.

"(3) REQUESTS FOR ISSUANCE OF PRODUCT CLASS-SPECIFIC RULE.—

"(A) IN GENERAL.—Any person may submit a request to the Secretary for the issuance of a product class-specific rule applicable to a qualified biological product and its class.

"(B) PRIORITY.—The Secretary—

"(i) in prioritizing among requests under this paragraph for a rule, shall consider likely market entry dates of biosimilars and the amount of time that will be needed to prepare the requested product class-specific rule; and

''(ii) may summarily reject frivolous or unsupported requests.

''(C) ISSUANCE OF RULE.—

''(i) IN GENERAL.—In response to a request under this paragraph, the Secretary shall carry out notice and comment rulemaking procedures in accordance with clause (ii).

''(ii) PROCEDURES.—To publish product class-specific rules under this paragraph, the Secretary shall, in response to a request under this paragraph—

''(I) publish in the Federal Register a concept paper setting forth the specific questions to be addressed in the product class-specific rule and invite comments on the concept paper from any interested persons;

''(II) accept comments on the concept paper for not less than 4 months;

''(III) consider the public comments on the concept paper;

''(IV) publish in the Federal Register the proposed product class-spe-

cific rule and invite comments on the proposed rule from any interested persons;

"(V) accept comments on the proposed rule for not less than 6 months;

"(VI) obtain the advice of the Biosimilars Advisory Committee with respect to the proposed rule; and

"(VII) except as provided in subparagraph (D), not later than 2 years after receipt of the initial request, publish in the Federal Register the final product class-specific rule or a determination that, given the current state of scientific and technical knowledge, it is not feasible to issue a product class-specific rule setting forth data that will ensure the safety, purity, and potency of biosimilars to be covered by the rule.

"(iii) REPORT TO CONGRESS.—If the Secretary determines under clause (ii)(VII) that it is not feasible to issue the final class-specific rule in the 2-year period fol-

lowing the date of the applicable initial request, the Secretary shall submit to Congress a report that describes why Secretary was unable to issue such final rule and the plan and timeline of the Secretary for issuing such final rule.

''(D) CONSOLIDATION OF REQUESTS.—The Secretary may consolidate requests submitted under this paragraph that refer to closely related products or product classes. If the Secretary chooses to consolidate such requests, the Secretary shall publish the final product class-specific rule or a determination described in subparagraph (C)(ii)(VII) not later than 30 months after receipt of the first request for a rule for any product in the class.

''(4) PRODUCT CLASS-SPECIFIC RULES.—

''(A) IN GENERAL.—A rule published under paragraph (3) shall describe the data and information that will be required in an application submitted under paragraph (1).

''(B) REQUIRED ELEMENTS.—At a minimum, a rule published under paragraph (3) shall require—

''(i) data demonstrating the consistency and robustness of the manufacturing process for the active ingredient or active ingredients of the biosimilar and the finished formulation of the biosimilar;

''(ii) data demonstrating the stability, compatibility (such as with excipients), and biological and physicochemical integrity of the active ingredient or active ingredients of the biosimilar;

''(iii) data from physical, chemical, and biological assays fully characterizing the biosimilar, in comparison with the reference product, at both the active ingredient or active ingredients and finished product levels;

''(iv) data from comparative nonclinical studies demonstrating that the biosimilar and the reference product have similar profiles in terms of pharmacokinetics, pharmacodynamics, toxicity, immunogenicity, and other relevant factors;

''(v) data from comparative clinical trials demonstrating that the biosimilar

and the reference product have similar profiles in terms of safety, purity, and potency, including pharmacokinetic studies, pharmacodynamic studies, immunogenicity studies, and trials of sufficient size and duration to demonstrate that the products are similar in their safety (in terms of nature, seriousness, and frequency of adverse reactions), purity, and potency profiles; and

''(vi) data regarding postmarket assessment and monitoring of safety, purity, and potency, including, as appropriate, clinical trials, tests to investigate immunogenicity, patient registries, and other surveillance measures.

''(5) REVISIONS TO RULES.—If a new condition of use is approved for a reference product after the latest publication of the final product class-specific rule applicable to such product, the Secretary shall promptly update and republish the rule in accordance with paragraphs (3) and (4) (irrespective of whether a request for such revision has been received under paragraph (3)(A)) to address the data and information that will be required in an applica-

tion under this subsection for approval of the new condition of use. The requirements of paragraph (2)(C) shall apply if the new condition of use is a new indication.

''(6) BIOSIMILARS ADVISORY COMMITTEE.—

''(A) ESTABLISHMENT.—The Secretary shall establish a Biosimilars Advisory Committee (in this paragraph referred to as the 'Committee').

''(B) DUTIES.—The Committee shall—

''(i) provide expert scientific advice and recommendations to the Secretary regarding the development and approval of biosimilars; and

''(ii) in formulating such advice and recommendations, provide interested persons with a reasonable opportunity to make written and oral presentations.

''(C) MEMBERSHIP.—

''(i) QUALIFICATIONS.—The Secretary shall appoint to serve on the Committee individuals with expertise on therapeutic biological products, including manufacturing, safety, effectiveness, and other relevant matters. The Secretary shall ensure that

the Committee consists of members with adequately diversified expertise and practical experience in such fields as clinical medicine, biological and physical sciences, pharmacoepidemiology and postmarket safety surveillance, and related professions.

''(ii) NOMINATIONS.—In appointing members of the Committee, the Secretary shall provide an opportunity for scientific, industry, and consumer organizations and the public to nominate such members.

''(iii) NONVOTING MEMBERS.—The Committee shall include, as nonvoting members, representatives of patient organizations, manufacturers of innovative biological products, and manufacturers of biosimilars.

''(iv) SUPPLEMENTAL MEMBERSHIP.—For the purpose of developing a product class-specific rule under paragraphs (3) and (4), the Secretary may supplement the membership of the Committee, or arrange for advice from another advisory committee, in order to obtain the ad-

vice of individuals with special expertise relating to any product under review.

''(7) TIME FRAMES FOR APPLICATION AND AUTHORIZATION.—

''(A) SUBMISSION OF APPLICATIONS.—No application for a biosimilar may be submitted under this subsection unless—

''(i) the Secretary has published under paragraph (3) a final product class-specific rule applicable to the reference product; and

''(ii) not less than 12 years have elapsed from the date on which the reference product was approved or licensed.

''(B) EFFECTIVE DATE OF APPROVAL.—Subject to subparagraph (C), approval of an application submitted under paragraph (1) shall not be made effective until at least 14 years have elapsed from the date on which the reference product was approved or licensed.

''(C) SIGNIFICANT CLINICAL BENEFIT.—Approval of an application submitted under paragraph (1) shall not be made effective until at least 16 years have elapsed from the date on

which the reference product was approved or licensed if—

"(i) during the 12-year period following the approval or licensing of the reference product, the Secretary approves a supplement to the new drug or biologics license application for the reference product that seeks approval to market the reference product for a new indication; and

"(ii) in the opinion of the Secretary, the new indication provides a significant clinical benefit.

"(D) SUPPLEMENT APPLICATION OF REFERENCE PRODUCT.—If, at any time following approval of the reference product, the holder of the approved reference product application submits a supplemental application with new clinical data (other than bioavailability data) to support a new condition of use (other than a new indication with a significant clinical benefit approved during the first 12 years after initial product approval), and those data are essential to approval of the supplemental application, the Secretary may not approve an application for a

biosimilar for the new condition of use for 3 years following approval of the supplement.

''(E) EXCLUSIVE APPROVAL PATHWAY.—The Secretary may not approve, under any other provision of law, a product that is claimed to be similar to or the same as a reference product.

''(F) APPROVAL OF BIOSIMILAR APPLICATION WITH RESPECT TO OLDER REFERENCE PRODUCTS.—Notwithstanding any other provision of this subsection, an application submitted under paragraph (1) that relies on a reference product approved more than 14 years before the date of enactment of this subsection may be made effective on the date that is the later of—

''(i) the publication of a product class-specific rule under paragraph (3) in which the reference product is included; or

''(ii) 1 year after the date of enactment of this subsection.

''(G) TRANSITION.—If, during the period following the approval of a reference product that was approved more than 14 years before the date of enactment of this subsection but before the publication of a product class-specific

rule under paragraph (3) in which the reference product is included, the holder of the approved reference product application obtains approval of a new indication with a significant clinical benefit as determined by the Secretary, approval of an application submitted under paragraph (1) that relies on such reference product may not be made effective under 16 years after the date of approval of the reference product.

''(8) PATENT NOTIFICATIONS AND LINKAGES.—

''(A) NOTIFICATION.—When an application for a biosimilar is submitted, the Secretary shall publish a notice in the Federal Register identifying—

''(i) the sponsor of the application of the reference product upon which the application for the biosimilar relies; and

''(ii) the name of the sponsor of the application for the biosimilar, or an agent designated by such sponsor to receive communications regarding patents.

''(B) INFORMATION FROM PATENT HOLDER.—

''(i) IN GENERAL.—A patent owner may—

"(I) request information from the person that submits an application for a biosimilar under paragraph (1) to ascertain whether such person's product or processes would infringe on a patent of the patent owner;

"(II) provide such person or its designee a notice of patents that may be infringed by the production or sale of the biosimilar, such as patents on compound (protein sequence), composition, host cell, nucleic acid, process of production, and method of treatment patents; or

"(III) indicate with such notification whether the patent holder is open to licensing the patent rights on a non-exclusive basis.

"(ii) NO DECLARATORY JUDGMENT.—A patent designated as available for licensure pursuant to clause (i)(III) may not be the subject of a declaratory judgment action brought by the biosimilar applicant prior to approval of the application for a biosimilar under this subsection.

''(C) WRITTEN EXPLANATION.—

''(i) IN GENERAL.—A person that submits an application for approval of a biosimilar under this subsection that requests approval prior to the expiration of a patent identified by a patent owner shall provide to such patent owner, a written explanation of—

''(I) why the patent identified in subparagraph (B)(i) would not be infringed by the approval of the application for the biosimilar; or

''(II) why the identified patent is invalid.

''(ii) COMPLIANCE.—With respect to process of manufacture patents, the biosimilar applicant must comply with the requirements of section 295 of title 35, United States Code.

''(D) APPROVAL DATE.—Approval of an application for a biosimilar submitted under this subsection may be effective on the applicable date described in paragraph (7) even if patent litigation has not concluded. If a patent is found valid and infringed before approval of the

application for a biosimilar, and the patent expires after the applicable effective date of the biosimilar application described in paragraph (7), approval of the biosimilar application may not be effective until the expiration of the infringed patent.

''(E) DECLARATORY JUDGMENT ACTION.—A person that submits an application for a biosimilar under this subsection may not commence a declaratory judgment action concerning a patent identified in subparagraph (B)(i) later than 18 months before the applicable effective date of the biosimilar application described in paragraph (7), or the date that is 60 days after providing the written explanation in subparagraph (C) of this paragraph, if such provision occurs during the 18-month period before the applicable effective date of the biosimilar application described in paragraph (7).

''(9) EXCLUSIVITY OF BIOSIMILARS.—The Secretary may not approve an application for a biosimilar that relies on a reference product for 1 year after the date of approval of the first biosimilar application that relies on such reference product.

''(l) PROPER NAME.—For purposes of this section:

''(1) BIOTECHNOLOGY-DERIVED THERAPEUTIC PROTEINS.—

''(A) IN GENERAL.—Subject to subparagraph (D), the term 'proper name', with respect to a biotechnology-derived therapeutic protein, means—

''(i) the name adopted for such protein by the United States Adopted Names Council if such name is a unique USAN; or

''(ii) if the biotechnology-derived therapeutic protein lacks a unique USAN, an official name designated pursuant to subparagraph (C).

''(B) UNIQUE USAN.—The term 'unique USAN', with respect to a biotechnology-derived therapeutic protein, means a name adopted for such protein by the United States Adopted Names Council that has not been adopted for any protein manufactured by a different person.

''(C) DESIGNATION.—The Secretary shall designate an official name for any biotechnology-derived therapeutic protein that lacks a unique USAN. Any official name designated under this subparagraph shall be the

only official name of that protein used in any official compendium published after such name has been designated. In no event, however, shall the Secretary designate an official name so as to infringe a valid trademark. Any designation under this subparagraph shall be made by rule in accordance with section 553 of title 5, United States Code.

''(D) EXCEPTION.—The term 'proper name', with respect to a biotechnology-derived therapeutic protein that was licensed by the Secretary prior to the effective date of the Affordable Biologics for Consumers Act, means the name adopted for such protein by the United States Adopted Names Council, irrespective of whether such name is a unique USAN.

''(2) OTHER BIOLOGICAL PRODUCTS.—The term 'proper name', with respect to a biological product that is not a biotechnology-derived therapeutic protein, means—

''(A) the official name designated by the Secretary for such biological product pursuant to section 508 of the Federal Food, Drug, and Cosmetic Act;

''(B) if there is no such official name and such biological product is an article recognized in an official compendium, the official title thereof in such compendium; or

''(C) if neither subparagraph (A) nor subparagraph (B) applies, the common or usual name, if any, of such biological product.

''(m) INTERCHANGEABILITY.—

''(1) IN GENERAL.—

''(A) NO DESIGNATION OF INTERCHANGEABILITY OR THERAPEUTIC EQUIVALENCE.—The Secretary may not designate a biosimilar as interchangeable with (or therapeutically equivalent to) the applicable reference product.

''(B) ASSESSMENT.—Not later than 2 years after the date of enactment of this subsection, and every 2 years thereafter, the Secretary shall assess the state of scientific and technical knowledge regarding the ability of the Food and Drug Administration to make a determination that a biosimilar is interchangeable with (or therapeutically equivalent to) a reference product on a product class basis.

''(2) DETERMINATION.—If the Secretary finds that the state of scientific and technical knowledge

enables the Food and Drug Administration to make a determination of interchangeability (or therapeutic equivalence) with respect to 1 or more product classes, then the Secretary shall submit a report to Congress that describes such findings and recommendations for statutory criteria that should govern such a determination.''.

(b) CONFIDENTIALITY.—Subsection (j) of section 351 of the Public Health Service Act (42 U.S.C. 262), as amended by subsection (a)(1), is further amended by adding at the end the following: ''The Secretary shall maintain the confidentiality of information submitted under this section for a biological product to the same extent and in the same manner as the Secretary maintains the confidentiality of information submitted under section 505 of the Federal Food, Drug, and Cosmetic Act for a drug.''.

(c) PATENT ACTIONS.—

(1) INFRINGEMENT ACTION.—Section 271(e)(2) of title 35, United States Code, is amended—

(A) in subparagraph (A), by striking '', or'' and inserting a comma;

(B) in subparagraph (B), by striking ''patent,'' and inserting ''patent, or''; and

(C) by adding after subparagraph (B) the following:

''(C) a written explanation described in section 351(k)(8)(C)(i) of the Public Health Service Act,''.

(2) PATENT TERM AUTHORITY.—Section 156(b) of title 35, United States Code, is amended by adding at the end before the period, the following: '', and shall extend to any product that is the subject of an application approved under section 351(k) of the Public Health Service Act''.

SEC. 3. AMENDMENTS TO FEDERAL FOOD, DRUG, AND COSMETIC ACT.

(a) LABELING.—

(1) UNIQUE NAME.—Section 502 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 352) is amended by adding at the end the following:

''(y) If it is a biotechnology-derived therapeutic protein, it was licensed under section 351 of the Public Health Service Act prior to the effective date of the Affordable Biologics for Consumers Act, it lacks a unique USAN, and its labeling fails to bear (i) its proper name (as defined in section 351(l) of the Public Health Service Act); (ii) its brand name or phrasing, approved by the Secretary, that adequately distinguishes it from other ap-

proved biotechnology-derived therapeutic proteins with the same proper name; and (iii) the following warning: 'Any change in _____, including a change in manufacturer, should be made cautiously and only if authorized by and supervised by the prescribing health care professional.', with the proper name of the product being inserted in the blank space. The requirement in the preceding sentence regarding the inclusion of a warning applies beginning on the date that is 180 days after the date of the enactment of the Affordable Biologics for Consumers Act.

''(z) If it is a biotechnology-derived therapeutic protein not subject to paragraph (y), and its labeling fails to include (i) its proper name (as defined in section 351(l) of the Public Health Service Act); and (ii) the following warning: 'This product shall not be dispensed in substitution for another biological product that was prescribed to be dispensed, unless such substitution was expressly authorized by and is supervised by the prescribing health care professional.'. In the case of such a protein that is a biosimilar licensed under section 351(k) of the Public Health Service Act, the warning required by the preceding sentence shall read as follows: 'This product shall not be dispensed in substitution for another biological product that was prescribed to be dispensed including

_____.', with the proprietary name and proper name of the reference product being inserted in the blank space.

''(aa) If it is a biosimilar approved under section 351(k) of the Public Health Service Act and the labeling—

''(1) is inconsistent with the labeling of the reference product (as referred to in such section 351(k));

''(2) does not accurately characterize the biosimilar or account for any differences between the biosimilar and the reference product;

''(3) does not describe any new data submitted in support of approval of the biosimilar since the date of approval of the reference product;

''(4) does not disclose any special safety concerns identified with respect to the biosimilar; or

''(5) omits any safety information, such as adverse events, that are identified with respect to, and included in the labeling of, the reference product, unless sponsor of such biosimilar justifies such omission to the Secretary.''.

(b) DISPENSING.—Section 503(b) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 353(b)) is amended by adding at the end the following:

''(6) A drug that is subject to paragraph (1) and is a biotechnology-derived therapeutic protein licensed under section 351 of the Public Health Service Act shall not be dispensed unless the prescription specifies the drug's proprietary name or, if the drug lacks a proprietary name, the drug's proper name (as defined in section 351(l) of such Act). The act of dispensing a drug contrary to the preceding sentence shall be deemed to be an act which results in the drug being misbranded while held for sale.''.

SEC. 4. REPORT TO CONGRESS.

Not later than 2 years after the date of the enactment of this Act, and every 2 years thereafter, the Secretary of Health and Human Services shall submit a report to the Congress making recommendations on whether it is feasible, in the state of scientific and technical knowledge (as of the date of such report), to approve applications under section 351(k) of the Public Health Service Act, as added by section 2 of this Act, for biological products that are claimed to be similar to vaccines, blood or plasma products or their derivatives, gene therapy, cell processing, naturally derived therapeutic proteins, or other biological products that do not contain biotechnology-derived therapeutic proteins as any active ingredient.

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